CASE REPORTS

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Cortisone and Thyroid Hyperplasia

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MOST OBSERVERS AGREE that in normal humans and rats, administration of cortisone depresses function of the thyroid gland,[2,4,6,7,9,12,14,16,17] as measured by a diminished uptake of I^{131} and a decrease in the serum content of protein-bound iodine. Whether the diminished thyroid function is the result of reduction in the amount of thyrotropin secreted by the pituitary, of interference with the utilization of thyrotropin, or of interference with the synthesis of thyrotoxin within the thyroid gland itself, or is due to other factors, is not yet clear.[1,2,6,14,15] It should be noted that some investigators question that cortisone depresses thyroid function,[3, 8, 11] and O'Neal and Heinbecker[13] have expressed doubt that it has any effect on the gland whatever. Because of the calorigenic action of cortisone, the basal metabolic rate may be reduced, normal or increased after cortisone therapy.[7, 10]

The authors know of no report in the literature of goiter arising during the course of treatment with corticotropin (ACTH) or cortisone. That occurred in the case here reported, but it is emphasized that a causal relationship between cortisone and goiter, although likely in this case, is unproven.

The patient, a housewife 47 years of age, consulted an allergist in November 1951, because of nasal congestion, mucoid nasal discharge and occasional sneezing for four years. Since the onset of a "head cold" in 1947, a troublesome non-productive cough had persisted. Occasional migraine had responded to Benadryl.® Examination showed a condition interpreted as allergic rhinitis. Intradermal skin tests were only mildly positive to environmental materials, foods and bacteria and were negative to pollens and molds. The tonsils had been removed. There was no evidence of sinusitis, and the ears were normal. The lungs were clear. No abnormality had been observed in an x-ray film of the chest in 1949. There was no enlargement of lymph nodes. The blood showed no eosinophilia. A beta hemolytic streptococcus grew on culture of material taken from the throat.

For the ensuing year, up to November 1952, the patient took potassium iodide (enteric coated), 0.3 gm. three times daily; thereafter, twice that amount daily until July 1953. No improvement was noticed from the iodine, but the patient was considerably better when she restricted or stopped smoking. Exacerbations occurred when the weather turned foggy or damp. In October 1952 the patient was sometimes awakened at night by the dry cough, and it was decided to try cortisone. The first day, 200 mg. was given by mouth in divided doses, the second day 100 mg., and diminishing doses thereafter until a maintenance daily dose of 12.5 mg. was reached in four weeks. Thereafter, for eight and a half months, until July 1953, the patient took from 12.5 to 37.5 mg. of cortisone daily, the dose varying according to the severity of symptoms.

In April 1953, the patient noticed a swelling in the neck. Upon examination on May 11, symmetrical enlargement of the thyroid gland was noted. There was some question of nodularity, but no tenderness, and no evidence of toxicity. The blood pressure was 120/80, and the heart was normal. Measurements of the circumference of the neck were as follows: May 11, 37 cm.; May 18, 35.5 cm.; May 25, 35.5 cm.; June 2, 34 cm.; June 22, 37 cm. On the last date, the patient complained of tightness in the neck and persistence of dry cough. The thyroid gland felt firmer, and for the first time puffiness was noted around the eyes. It was interpreted as being due, perhaps, to early myxedema. It was thought likely that the cough was due to pressure of the thyroid gland on the trachea. On June 24, 1953, the basal metabolic rate was minus 10, minus 15.

In preparation for operation, treatment with cortisone and potassium iodide was discontinued and corticotropin was injected intramuscularly in daily dosage of 20 units of Acthar® on July 7, 8, 9, 10, 13 and 14, 1953. The patient was admitted to hospital July 14. A roentgenogram of the chest showed no substernal goiter or other abnormality. The patient noted respiratory pressure symptoms with the neck either extended or flexed. She thought there had been a gradual change in pitch of the voice but no

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definite hoarseness. A diagnosis of bilateral, multinodular, non-toxic goiter was made.

The blood pressure was 140/82 and the pulse rate 78. Results of urinalysis were within normal limits. Erythrocytes numbered 4.75 million per cu. mm. of blood and the hemoglobin value was 96 per cent. Leukocytes numbered 20,400—82 per cent segmental cells, 4 per cent stab forms and 14 per cent lymphocytes. The result of a Kline test was negative.

Subtotal thyroidectomy was carried out and the gland was observed to be symmetrically enlarged, homogeneous and relatively avascular. Pressure symptoms were relieved by operation and the voice returned to its normal pitch. Puffiness about the eyes was accentuated for several days after operation, then receded and in two weeks disappeared. On September 23, 1953, the basal metabolic rate was minus 4, minus 12.

Pathologist's report. The tissue removed weighed 35 grams. The gross section was reddish gray, uniform, and of beefsteak consistency throughout. Microscopic sections from four different areas showed small acini, which for the most part were empty and lined by tall epithelial cells (Figure 1). Many acini contained papillary infoldings. The epithelial cells appeared to be actively secreting an eosinophilic, amorphous material. The stroma was sparse and there was no lymphocytic infiltration whatsoever. A diagnosis of primary hyperplasia was made.

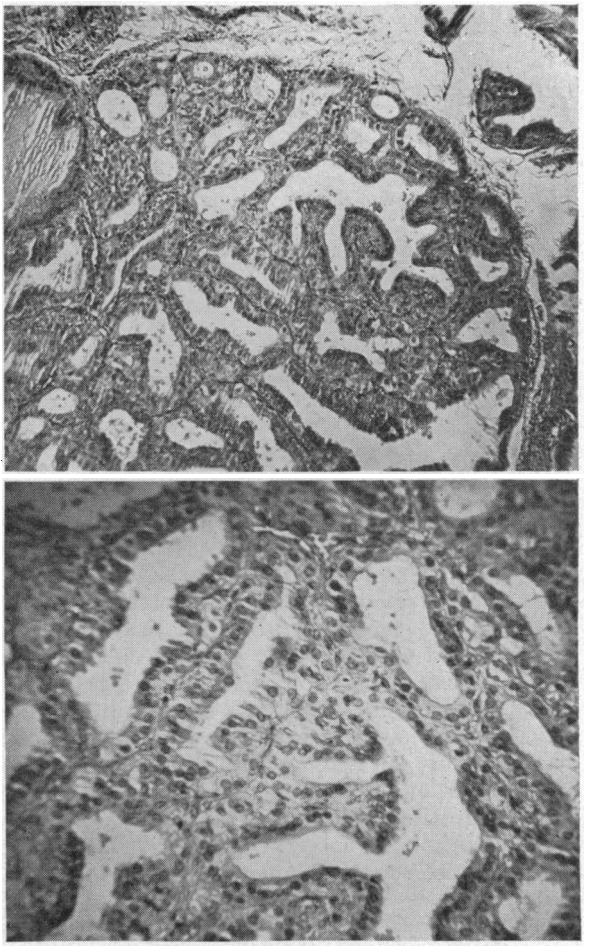

Figure 1.—Hyperplasia of thyroid gland, hematoxylin-eosin stained, green filter. ***Upper,*** **×100;** ***lower,*** **×225.**

DISCUSSION

Although no similar clinical case has been recorded, Halmi and Barker[5] in August 1952, showed photomicrographs of hyperplastic thyroid tissue removed from rats which had been injected with 2 to 5 mg. of cortisone daily over periods of from 20 to 83 days. Pair-fed control animals showed no hyperplasia. More recent experiments by O'Neal and Heinbecker[13] did not confirm the results of Halmi and Barker. The subject is confused by variations in the conditions in experiments, such as differences in the iodine content of the diet, and by the ofttimes grossly excessive doses, by body weight, of corticotropin or cortisone given to the animals as compared to doses for humans.

SUMMARY AND CONCLUSION

Hyperplastic goiter occurred in a woman who was under prolonged treatment with cortisone for allergic rhinitis. There was no evidence of hyperthyroidism, but the histologic appearance of a portion of the gland removed resembled that of primary hyperplasia. Similar histologic structure was noted by Halmi and Barker[5] in rats under treatment with cortisone.

It is suggested that there may have been a relationship between cortisone therapy and the development of goiter in the case reported. Because of the current state of ignorance concerning this possible relationship and in light of the possibility that simply discontinuing hormonal therapy might bring relief, surgeons should be slow to remove diffuse goiters arising in similar circumstances.

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Hemophilus Influenza Epiglottitis in a 12-year-old Child

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A 12-YEAR-OLD BOY was admitted to the communicable disease unit of the Los Angeles County General Hospital because of difficulty in swallowing and breathing of one day's duration.

The patient had been entirely well until two days before admittance when he noted a slight stiffness of both legs which subsided the same day. The following day fever, sore throat and general malaise developed. When he awoke on the morning of the day of admittance the patient noted, in addition, pronounced difficulty in breathing and swallowing. At times he gasped for air but was not cyanotic. When he attempted to swallow water it was forced out through the nose. There was no headache, backache or peripheral weakness, and no visual disturbances were noted. A physician who had examined the patient referred him to the hospital with a provisional diagnosis of bulbar poliomyelitis. So far as could be determined the patient had not been in contact with anyone having a communicable disease.

Except for eczema in infancy and allergic rhinitis in childhood, the patient had always been in excellent health.

When examined upon admittance he was observed to be mentally oriented, acutely ill and in pronounced respiratory distress, but not cyanotic. He preferred sitting up to reclining, and the mouth was kept open. Swallowing was difficult and painful. The voice was moderately hoarse, but there was no stridor. The temperature was 103.8° F., the pulse rate 126 and respirations 30 per minute. The blood pressure was 120/80 (mm. mercury).

The skin and mucous membranes were normal and there were no palpable nodes. The throat was bright red. No pooling of secretions was noted. The gag reflex was not impaired. Only on indirect laryngoscopy was the epiglottis visible. It was red and edematous. There was no formation of membrane about it. The neck was supple, but there was pronounced tenderness along the anterior cervical chain.

Upon examination of the chest, moderate intercostal retractions were noted and there was occasional use of the accessory muscles of respiration. Aeration was poor (vital capacity 525 cc.), but the lungs were clear except for transmitted rhonchi. Thoracic and abdominal respiratory excursions were dissociated. The heart and abdomen were normal. The extremities showed no weakness, all reflexes were equal and active, and no sensory abnormalities were noted.

The hemoglobin content of the blood was 12.0 gm. per 100 cc. Leukocytes numbered 22,450 per cu. mm. and 86 per cent were polymorphonuclear cells. The urine was normal except for 1 plus albumin. The cerebrospinal fluid pressure was 130 mm. of mercury. The fluid contained 4 cells per cu. mm. (lymphocytes), and the protein and sugar content was normal. Hemophilus influenzae, type B, grew on cultures of blood and of material from the nasopharynx.

The patient was placed in a croupette with oxygen. Fluids were given intravenously and antibiotics (penicillin, streptomycin, chloromycetin, and sulfa drugs) parenterally. Respiratory distress increased greatly in the next hour and tracheotomy was performed. There was moderate immediate relief and by the next morning the patient was greatly improved. He became afebrile on the fourth day of hospitalization and was discharged on the eighth day.

COMMENT

The present case is reported because of the infrequent occurrence of H. influenzae epiglottitis in this age group. Indirect laryngoscopy was required to visualize the epiglottis. The difficulty in respiration, phonation and deglutition in a febrile patient might lead erroneously to diagnosis of bulbar poliomyelitis.

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